Barb O'Bryen

RECEIVED
APR 15 2003
(STIC)

Access DB# 91609

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Rebecca Cook Examiner #: [redacted] Date: 4/15/03
Art Unit: 1614 Phone Number 308-4724 Serial Number: 10/069,914
Mail Box and Bldg/Room Location: Crus 2 DO1 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): Lyndell Kelly

Earliest Priority Filing Date: 12/30/99

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please provide structure of cyanohydroxybutene
& Search it to treat pancreatic disease (general)
(see claims 1, 6-7, 13), cancer & pancreatitis.

What are acinar cells.

Thanks
Rebecca

Point of Contact:
Barb O'Bryen
Technical Information Specialist
STIC CM1 6A05 308-4291

****

STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher: BOB	NA Sequence (#)		STN	298
Searcher Phone #:	AA Sequence (#)		Dialog	
Searcher Location:	Structure (#)	3	Questel/Orbit	
Date Searcher Picked Up:	Bibliographic		Dr.Link	
Date Completed: 4-28-03	Litigation		Lexis/Nexis	
Searcher Prep & Review Time: 30	Fulltext		Sequence Systems	
Clerical Prep Time:	Patent Family		WWW/Internet	Medline Plus
Online Time: 39	Other		Other (specify)	Chem Draw

PTO-1590 (8-01)

MEDLINEplus® Health Information

Merriam-Webster

Medical Dictionary

One entry found for **acinar**.

Main Entry: ac·i·nar
Pronunciation: 'as-&-n&r, -"när
Function: *adjective*
: of, relating to, or comprising an acinus <pancreatic *acinar* cells>

Search here for another word:

SEARCH acinus Look it up

Merriam-Webster

Pronunciation Key

\&\ as **a** and **u** in **abut**	\ch\ as **ch** in **ch**in	\o\ as **aw** in l**aw**
\ᵊ\ as **e** in kitt**e**n	\e\ as **e** in b**e**t	\oi\ as **oy** in b**oy**
\&r\ as **ur** and **er** in f**ur**th**er**	\E\ as **ea** in **ea**sy	\th\ as **th** in **th**in
\a\ as **a** in **a**sh	\g\ as **g** in **g**o	\th\ as **th** in **th**e
\A\ as **a** in **a**ce	\i\ as **i** in h**i**t	\ü\ as **oo** in l**oo**t
\ä\ as **o** in m**o**p	\I\ as **i** in **i**ce	\u\ as **oo** in f**oo**t
\au\ as **ou** in **ou**t	\j\ as **j** in **j**ob	\y\ as **y** in **y**et
	\[ng]\ as **ng** in si**ng**	\zh\ as **si** in vi**si**on
	\O\ as **o** in g**o**	

MEDLINEplus® Health Information

Merriam-Webster

Medical Dictionary

One entry found for **acinus**.

Main Entry: **aci·nus**
Pronunciation: 'as-&-n&s, &-'sI-
Function: *noun*
Inflected Form(s): *plural* **aci·ni** /-"nI/
: any of the small sacs or alveoli that terminate the ducts of some exocrine glands and are lined with secretory cells

Search here for another word:

SEARCH [ ] Look it up

Merriam-Webster

Pronunciation Key

\&\ as **a** and **u** in **abut**	\ch\ as **ch** in **chin**	\o\ as **aw** in **law**
\$^{&}$\ as **e** in **kitten**	\e\ as **e** in **bet**	\oi\ as **oy** in **boy**
\&r\ as **ur** and **er** in **further**	\E\ as **ea** in **easy**	\th\ as **th** in **thin**
\a\ as **a** in **ash**	\g\ as **g** in **go**	\th\ as **th** in **the**
\A\ as **a** in **ace**	\i\ as **i** in **hit**	\ü\ as **oo** in **loot**
\ä\ as **o** in **mop**	\I\ as **i** in **ice**	\u\ as **oo** in **foot**
\au\ as **ou** in **out**	\j\ as **j** in **job**	\y\ as **y** in **yet**
	\[ng]\ as **ng** in **sing**	\zh\ as **si** in **vision**
	\O\ as **o** in **go**	

-Johns Hopkins Pathology

FUNCTION

The pancreas can also be thought of as having different functional components, the endocrine and exocrine parts. Tumors can arise in either part. However, the vast majority arise in the exocrine (also called non-endocrine) part. Since the parts have different normal functions, when tumors interfere with these functions, different kinds of symptoms will occur.

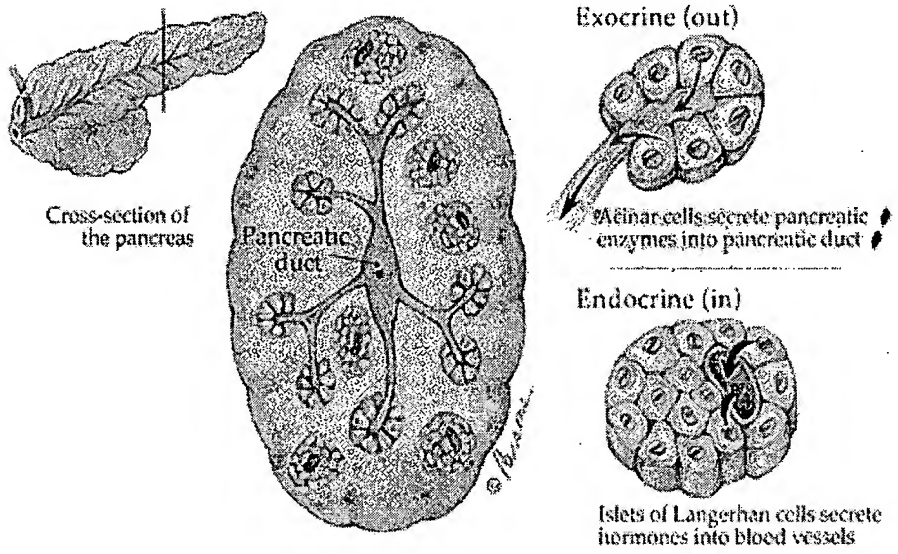
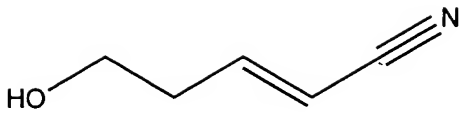


Fig. 1-4

Islets of Langerhans-	These are the endocrine (endo= within) cells of the pancreas that produce and secrete hormones into the bloodstream. The pancreatic hormones, insulin and glucagon, work together to maintain the proper level of sugar in the blood. The sugar, glucose, is used by the body for energy.
Acinar cells-	These are the exocrine (exo= outward) cells of the pancreas that produce and transport chemicals that will exit the body through the digestive system. The chemicals that the exocrine cells produce are called enzymes. They are secreted in the duodenum where they assist in the digestion of food.

CONTINUED

* No two patients with pancreas cancer are identical. The appropriate treatment of individual cases varies greatly depending o the patient's medical and surgical history. The information expressed in this Web page is not medical advice. It is meant only t educate health care professionals and patients about the current status of treatment and research at Hopkins. Before making an medical decisions, patients are advised to consult with their personal physicians.



cyanohydroxybutene

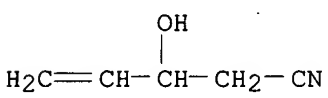
ChemDraw's interpretation

514/526

THIS PAGE BLANK (USPTO)

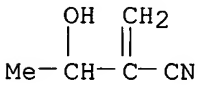
```
=> fil reg; d ide
FILE 'REGISTRY' ENTERED AT 14:36:24 ON 28 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   27 APR 2003  HIGHEST RN 506405-59-0
DICTIONARY FILE UPDATES:  27 APR 2003  HIGHEST RN 506405-59-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf


L5   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   27451-36-1 REGISTRY
CN   4-Pentenenitrile, 3-hydroxy- (7CI, 8CI, 9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   1-Cyano-2-hydroxy-3-butene
CN   2-Hydroxy-3-butenyl cyanide
CN   3-Hydroxy-4-cyano-1-butene
CN   3-Hydroxy-4-pentenenitrile
FS   3D CONCORD
MF   C5 H7 N O
CI   COM
LC   STN Files:   AGRICOLA, BEILSTEIN*, BIOSIS, CA, CANCERLIT, CAOLD, CAPLUS,
       CASREACT, CHEMINFORMRX, MEDLINE, RTECS*, SPECINFO, TOXCENTER, USPATFULL
         (*File contains numerically searchable property data)
```

applicant should be more specific about which cyanohydroxy-butene this he's talking about



```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

             54 REFERENCES IN FILE CA (1957 TO DATE)
              1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             54 REFERENCES IN FILE CAPLUS (1957 TO DATE)
              2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)


=> d ide 1-2

L11  ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2003 ACS
RN   19362-94-8  REGISTRY
CN   Butanenitrile, 3-hydroxy-2-methylene- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Butyronitrile, 3-hydroxy-2-methylene- (8CI)
```

OTHER NAMES:
CN .alpha.-(1-Hydroxyethyl)acrylonitrile
CN 2-(1-Hydroxyethyl)acrylonitrile
CN 2-Cyano-3-hydroxy-1-butene
CN 3-Hydroxy-2-methylenebutyronitrile
FS 3D CONCORD
DR 138664-36-5
MF C5 H7 N O
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX, CHEMLIST, IFICDB, IFIPAT, IFIUDB, SPECINFO, USPATFULL
(*File contains numerically searchable property data)

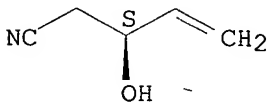


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

24 REFERENCES IN FILE CA (1957 TO DATE)
24 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L11 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN **6071-81-4** REGISTRY
CN 4-Pentenenitrile, 3-hydroxy-, (3S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 4-Pentenenitrile, 3-hydroxy-, (S)- (8CI)
OTHER NAMES:
CN (S)-1-Cyano-2-hydroxy-3-butene
CN Crambene
FS STEREOSEARCH
MF C5 H7 N O
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CHEMINFORMRX, NIOSHTIC, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

25 REFERENCES IN FILE CA (1957 TO DATE)
26 REFERENCES IN FILE CAPLUS (1957 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> fil reg; d stat que l10
FILE 'REGISTRY' ENTERED AT 14:59:11 ON 28 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 27 APR 2003 HIGHEST RN 506405-59-0
DICTIONARY FILE UPDATES: 27 APR 2003 HIGHEST RN 506405-59-0

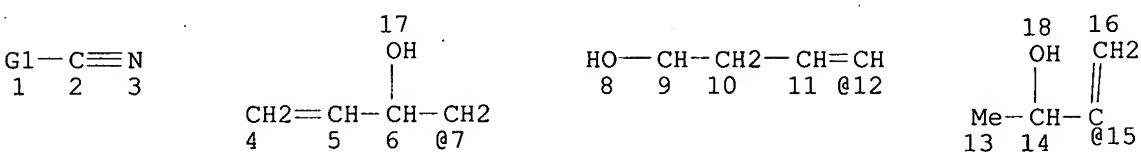
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

L8 STR



VAR G1=7/12/15
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

this structure would retrieve any of the 3 cyanohydroxy butenes

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
L10 19 SEA FILE=REGISTRY SSS FUL L8

100.0% PROCESSED 9865 ITERATIONS 19 ANSWERS
SEARCH TIME: 00.00.01

=> fil capl; d que nos l15; d que nos l17

FILE 'CAPLUS' ENTERED AT 14:59:13 ON 28 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 28 Apr 2003 VOL 138 ISS 18
FILE LAST UPDATED: 27 Apr 2003 (20030427/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L8              STR
L10          19 SEA FILE=REGISTRY SSS FUL L8
L12         143 SEA FILE=CAPLUS ABB=ON  L10
L14      102536 SEA FILE=CAPLUS ABB=ON  PANCREA? OR ACINAR
L15          12 SEA FILE=CAPLUS ABB=ON  L12 AND L14
```

```
L8              STR
L10          19 SEA FILE=REGISTRY SSS FUL L8
L12         143 SEA FILE=CAPLUS ABB=ON  L10
L16       75885 SEA FILE=CAPLUS ABB=ON  (DIABET? OR ANTIDIABET?)/OBI
L17           0 SEA FILE=CAPLUS ABB=ON  L12 AND L16
```

```
=> fil medl; d que nos l26

FILE 'MEDLINE' ENTERED AT 14:59:13 ON 28 APR 2003
```

FILE LAST UPDATED: 26 APR 2003 (20030426/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L8              STR
L10          19 SEA FILE=REGISTRY SSS FUL L8
L22          16 SEA FILE=MEDLINE ABB=ON  L10 OR CYANOHYDROXYBUTENE
L23       76735 SEA FILE=MEDLINE ABB=ON  PANCREATIC DISEASES+NT/CT OR CARCINOMA
                , ACINAR CELL/CT
L24        6477 SEA FILE=MEDLINE ABB=ON  PANCREAS/CT(L)PA/CT
L26           9 SEA FILE=MEDLINE ABB=ON  L22 AND (L23 OR L24)
```

```
=> fil embase; d que nos l33

FILE 'EMBASE' ENTERED AT 14:59:15 ON 28 APR 2003
```


FILE COVERS 1974 TO 24 Apr 2003 (20030424/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L8              STR
L10          19 SEA FILE=REGISTRY SSS FUL L8
L29          15 SEA FILE=EMBASE ABB=ON  L10 OR CYANOHYDROXYBUTENE OR CYANO(1W)H
                YDROXY(1W)BUTENE
L30        4045 SEA FILE=EMBASE ABB=ON  ACINAR CELL/CT
L31         432 SEA FILE=EMBASE ABB=ON  ACINAR CELL CARCINOMA/CT
L32       66664 SEA FILE=EMBASE ABB=ON  PANCREAS DISEASE+NT/CT
L33           5 SEA FILE=EMBASE ABB=ON  L29 AND (L30 OR L31 OR L32)
```

```
=> fil toxcenter; d que nos l37

FILE 'TOXCENTER' ENTERED AT 14:59:16 ON 28 APR 2003
COPYRIGHT (C) 2003 ACS

FILE COVERS 1907 TO 22 Apr 2003 (20030422/ED)

This file contains CAS Registry Numbers for easy and accurate substance
identification.

TOXCENTER has been enhanced with new files segments and search fields.
See HELP CONTENT for more information.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/summ2003.html
for a description on changes.

L8              STR
L10          19 SEA FILE=REGISTRY SSS FUL L8
L34          74 SEA FILE=TOXCENTER ABB=ON  L10 OR CYANOHYDROXYBUTENE OR
                CYANO(1W)HYDROXY(1W)BUTENE
L35       53730 SEA FILE=TOXCENTER ABB=ON  PANCRE? OR ACINAR OR ACINUS
L36       63250 SEA FILE=TOXCENTER ABB=ON  CYSTIC FIBROSIS OR DIABET? OR
                ANTIDIABET?
L37          33 SEA FILE=TOXCENTER ABB=ON  L34 AND (L35 OR L36)
```

```
=> fil drugu; d que nos l42
FILE 'DRUGU' ENTERED AT 15:06:52 ON 28 APR 2003
COPYRIGHT (C) 2003 THOMSON DERWENT

FILE LAST UPDATED: 22 APR 2003       <20030422/UP>
>>>  DERWENT DRUG FILE (SUBSCRIBER)  <<<

>>>  SDI'S MAY BE RUN WEEKLY OR MONTHLY AS OF JUNE 2001.  <<<
>>>  (WEEKLY IS THE DEFAULT). FOR PRICING INFORMATION     <<<
>>>  SEE HELP COST                                       <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<


L8              STR
L10          19 SEA FILE=REGISTRY SSS FUL L8
L39           5 SEA FILE=DRUGU ABB=ON  L10 OR CYANOHYDROXYBUTENE OR CYANO(1W)HY
                DROXY(1W)BUTENE
```

```
L40        45412 SEA FILE=DRUGU ABB=ON  PANCRE? OR ACINAR OR ACINUS
L41        38426 SEA FILE=DRUGU ABB=ON  CYSTIC FIBROSIS OR DIABET? OR ANTIDIABET
                 ?
L42            3 SEA FILE=DRUGU ABB=ON  L39 AND (L40 OR L41)


=> fil biosis; d que nos l46

FILE 'BIOSIS' ENTERED AT 15:06:53 ON 28 APR 2003
COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC.(R)

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 23 April 2003 (20030423/ED)



L8                 STR
L10           19 SEA FILE=REGISTRY SSS FUL L8
L43           51 SEA FILE=BIOSIS ABB=ON  L10 OR CYANOHYDROXYBUTENE OR CYANO(1W)H
                 YDROXY(1W)BUTENE
L44       194006 SEA FILE=BIOSIS ABB=ON  PANCRE? OR ACINAR OR ACINUS
L45       212117 SEA FILE=BIOSIS ABB=ON  CYSTIC FIBROSIS OR DIABET? OR ANTIDIABE
                 T?
L46           17 SEA FILE=BIOSIS ABB=ON  L43 AND (L44 OR L45)


=> fil wpids; d que nos l50

FILE 'WPIDS' ENTERED AT 15:06:54 ON 28 APR 2003
COPYRIGHT (C) 2003 THOMSON DERWENT

FILE LAST UPDATED:          16 APR 2003      <20030416/UP>
MOST RECENT DERWENT UPDATE:     200325        <200325/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

    Due to data production problems in updates 24 and 25
    the WPI file had to be reset to update 200323 on April 24
    and the corrected updates were reloaded.
    SDIs for update 24 were rerun. The previous SDI run for 24 has
    been credited.
    We also recommend to recreate answer sets dated between April 10
    and 24.  Charges incurred to accomplish this will be credited of
    course.

>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS  <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<
```

```
L47           3 SEA FILE=WPIDS ABB=ON  CYANOHYDROXYBUTENE OR CYANO(1W)HYDROXY(1
                W)BUTENE OR CYANO(W)HYDROXYBUTENE OR CYANOHYDROXY(W)BUTENE
L48        8726 SEA FILE=WPIDS ABB=ON  PANCRE? OR ACINAR OR ACINUS
L49       24870 SEA FILE=WPIDS ABB=ON  CYSTIC FIBROSIS OR DIABET? OR ANTIDIABET
                ?
L50           1 SEA FILE=WPIDS ABB=ON  L47 AND (L48 OR L49)

=> fil uspatf; d que nos l56

FILE 'USPATFULL' ENTERED AT 15:06:56 ON 28 APR 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 24 Apr 2003 (20030424/PD)
FILE LAST UPDATED: 24 Apr 2003 (20030424/ED)
HIGHEST GRANTED PATENT NUMBER: US6553568
HIGHEST APPLICATION PUBLICATION NUMBER: US2003079264
CA INDEXING IS CURRENT THROUGH 24 Apr 2003 (20030424/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 24 Apr 2003 (20030424/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2003

>>>  USPAT2 is now available.  USPATFULL contains full text of the     <<<
>>>  original, i.e., the earliest published granted patents or         <<<
>>>  applications.  USPAT2 contains full text of the latest US         <<<
>>>  publications, starting in 2001, for the inventions covered in     <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original     <<<
>>>  published document but also a list of any subsequent              <<<
>>>  publications.  The publication number, patent kind code, and      <<<
>>>  publication date for all the US publications for an invention     <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL   <<<
>>>  records and may be searched in standard search fields, e.g., /PN, <<<
>>>  /PK, etc.                                                         <<<

>>>  USPATFULL and USPAT2 can be accessed and searched together        <<<
>>>  through the new cluster USPATALL.  Type FILE USPATALL to          <<<
>>>  enter this cluster.                                               <<<
>>>                                                                    <<<
>>>  Use USPATALL when searching terms such as patent assignees,       <<<
>>>  classifications, or claims, that may potentially change from     <<<
>>>  the earliest to the latest publication.                           <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.


L8              STR
L10            19 SEA FILE=REGISTRY SSS FUL L8
L21             9 SEA FILE=USPATFULL ABB=ON  L10 OR CYANOHYDROXYBUTENE/IT
L51             4 SEA FILE=USPATFULL ABB=ON  CYANOHYDROXYBUTENE OR CYANO(1W)HYDRO
                  XY(1W)BUTENE OR CYANO(W)HYDROXYBUTENE OR CYANOHYDROXY(W)BUTENE
L52             1 SEA FILE=USPATFULL ABB=ON  (CYANO(1W)HYDROXY(1W)BUTENE OR
                  CYANO(W)HYDROXYBUTENE OR CYANOHYDROXY(W)BUTENE)/IT
L53            11 SEA FILE=USPATFULL ABB=ON  (L21 OR L51 OR L52)
L54         51495 SEA FILE=USPATFULL ABB=ON  PANCRE? OR ACINAR OR ACINUS OR
                  CYSTIC FIBROSIS OR DIABET? OR ANTIDIABET?
L55          8753 SEA FILE=USPATFULL ABB=ON  (PANCRE? OR ACINAR OR ACINUS OR
                  CYSTIC FIBROSIS OR DIABET? OR ANTIDIABET?)/IT
L56             0 SEA FILE=USPATFULL ABB=ON  L53 AND (L54 OR L55)

=> dup rem l15,l26,l42,l46,l37,l33,l50
```

FILE 'CAPLUS' ENTERED AT 15:06:57 ON 28 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 15:06:57 ON 28 APR 2003

FILE 'DRUGU' ENTERED AT 15:06:57 ON 28 APR 2003
COPYRIGHT (C) 2003 THOMSON DERWENT

FILE 'BIOSIS' ENTERED AT 15:06:57 ON 28 APR 2003
COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'TOXCENTER' ENTERED AT 15:06:57 ON 28 APR 2003
COPYRIGHT (C) 2003 ACS

FILE 'EMBASE' ENTERED AT 15:06:57 ON 28 APR 2003
COPYRIGHT (C) 2003 Elsevier Science B.V. All rights reserved.

FILE 'WPIDS' ENTERED AT 15:06:57 ON 28 APR 2003
COPYRIGHT (C) 2003 THOMSON DERWENT
PROCESSING COMPLETED FOR L15
PROCESSING COMPLETED FOR L26
PROCESSING COMPLETED FOR L42
PROCESSING COMPLETED FOR L46
PROCESSING COMPLETED FOR L37
PROCESSING COMPLETED FOR L33
PROCESSING COMPLETED FOR L50
L57 23 DUP REM L15 L26 L42 L46 L37 L33 L50 (57 DUPLICATES REMOVED)
ANSWERS '1-12' FROM FILE CAPLUS
ANSWERS '13-15' FROM FILE MEDLINE
ANSWER '16' FROM FILE DRUGU
ANSWERS '17-23' FROM FILE BIOSIS

=> d ibib ab hitstr 1-12; d iall 13=23

L57 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 2001:167801 CAPLUS
DOCUMENT NUMBER: 134:202685
TITLE: Administration of cyanohydroxybutene for the treatment of **pancreatic** diseases
INVENTOR(S): Kelly, E. Lyndell
PATENT ASSIGNEE(S): Australia
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

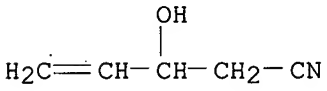
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001015690	A1	20010308	WO 2000-AU1026	20000830
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000068102	A5	20010326	AU 2000-68102	20000830

EP 1221951 A1 20020717 EP 2000-955960 20000830
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
PRIORITY APPLN. INFO.: AU 1999-2536 A 19990830
WO 2000-AU1026 W 20000830

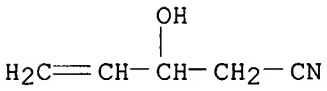
AB The invention relates to the administration of cyanohydroxybutene (CHB) to eliminate **acinar** cells in a subject. S.c. injection of CHB at a sub-lethal dosage caused apoptosis of the substantially entire population of **acinar** cells. The **pancreatic** lesion has marked early edema with limited inflammatory infiltration, rapid synchronous onset of **acinar** cell apoptosis and advanced atrophy with a severely limited regenerative response. There are further provided methods of treatment of **acinar** cell carcinoma and **pancreatitis**.

IT **27451-36-1 27451-36-1D**, ligand conjugates
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(administration of cyanohydroxybutene for the treatment of **pancreatic** diseases)

RN 27451-36-1 CAPLUS
CN 4-Pentenenitrile, 3-hydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 27451-36-1 CAPLUS
CN 4-Pentenenitrile, 3-hydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 3
ACCESSION NUMBER: 1998:351185 CAPLUS
DOCUMENT NUMBER: 129:76144
TITLE: Induction of apoptosis in **pancreatic** **acinar** cells reduces the severity of acute **pancreatitis**
AUTHOR(S): Bhatia, Madhav; Wallig, Matthew A.; Hofbauer, Bernd; Lee, Hong-Sik; Frossard, Jean-Louis; Steer, Michael L.; Saluja, Ashok K.
CORPORATE SOURCE: Department of Surgery, Beth Israel Deaconess Medical Center and Harvard Medical School, Harvard Digestive Diseases Center, Boston, MA, 02215, USA
SOURCE: Biochemical and Biophysical Research Communications (1998), 246(2), 476-483
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

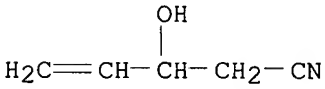
AB 1-Cyano-2-hydroxy-3-butene (CHB) has been reported to cause cell death in rat **pancreatic** acini. In this report, we describe the time-dependent effects of CHB on mouse **acinar** cell apoptosis and the effects of CHB-induced **acinar** cell apoptosis on the severity

IDS

of secretagogue-induced acute **pancreatitis** in mice. CHB administration to mice resulted in a time-dependent increase in **pancreatic** apoptosis, which was maximal 12 h after CHB administration. The severity of **pancreatitis** was significantly reduced by prior CHB administration and maximal protection was obsd. when the caerulein injections were started 12 h after CHB administration. These observations indicate that induction of apoptosis can reduce the severity of **pancreatitis** and they suggest that induction of **pancreatic acinar** cell apoptosis may be beneficial in the clin. management of acute **pancreatitis**.

IT **27451-36-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(apoptosis induction in **pancreatic acinar** cells reduces acute **pancreatitis** severity)

RN 27451-36-1 CAPLUS
CN 4-Pentenenitrile, 3-hydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 4
ACCESSION NUMBER: 1998:404740 CAPLUS
DOCUMENT NUMBER: 129:94931
TITLE: Induction of rat **pancreatic** glutathione S-transferase and quinone reductase activities by a mixture of glucosinolate breakdown derivatives found in Brussels sprouts
AUTHOR(S): Wallig, M. A.; Kingston, S.; Staack, R.; Jeffery, E. H.
CORPORATE SOURCE: Department of Veterinary Pathobiology, University of Illinois, Urbana, IL, 61802, USA
SOURCE: Food and Chemical Toxicology (1998), 36(5), 365-373
CODEN: FCTOD7; ISSN: 0278-6915
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

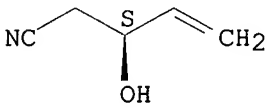
AB The chemoprotective effects of cruciferous vegetables against cancer has been linked to the induction of detoxification enzymes, including the phase II enzymes, glutathione S-transferase (GST) and quinone reductase (QR). Four glucosinolate breakdown products found in Brussels sprouts and previously shown individually to affect detoxification enzymes - (1-cyano-2-hydroxy-3-butene (Crambene), indole-3-carbinol (I3C), phenylethyl isothiocyanate (PEITC) and 1-isothiocyanato-3-(methylsulfinyl)-propane (IBN))-were administered to male F344 rats by esophageal intubation for 7 days both as a mixt. and individually to assess the effect of these compds. on GST and QR activity in the **pancreas**, an organ previously shown to be affected by cruciferous diets. The doses of each compd. in the mixt. (50 mg Crambene/kg, 56 mg 13C/kg, 0.1 mg PEITC/kg and 38 mg IBN/kg) were chosen to represent the relative proportions of the parent glucosinolate for each compd. in Brussels sprouts and shown to be below the toxic threshold for all the compds. In rats receiving the mixt., **pancreatic** QR and GST activities were elevated 31- and 1.7-fold, resp., while glutathione (GSH) was elevated threefold. On an individual basis, Crambene alone caused a 21-fold elevation of QR and 1.5-fold elevation of GST activities, while

pancreatic GSH was elevated by both Crambene and PEITC 2.6-and twofold, resp. No other significant effects of individual components were found. When the mixt. was administered at 60% of the original dose, **pancreatic** QR and GST activities were elevated 12- and 1.4-fold, resp., and **pancreatic** GSH was elevated 1.5-fold. At 20% of the original dose, **pancreatic** GSH was unaffected and QR and GST activities were elevated 2.7- and 1.3-fold, resp. The results of these studies suggest that a diet rich in cruciferous vegetables may produce phase II enzyme induction in the **pancreas**, and that Crambene may be the most active component.

IT **6071-81-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(induction of rat **pancreatic** glutathione S-transferase and quinone reductase activities by a mixt. of glucosinolate breakdown derivs. found in Brussels sprouts)

RN 6071-81-4 CAPLUS
CN 4-Pentenenitrile, 3-hydroxy-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 5
ACCESSION NUMBER: 1998:276573 CAPLUS
DOCUMENT NUMBER: 129:24940
TITLE: The cruciferous nitrile, crambene, induces rat hepatic and **pancreatic** glutathione S-transferases
AUTHOR(S): March, Thomas H.; Jeffery, Elizabeth H.; Wallig, Matthew A.
CORPORATE SOURCE: Department of Food Science and Human Nutrition, University of Illinois, Urbana, IL, 61802, USA
SOURCE: Toxicological Sciences (1998), 42(2), 82-90
CODEN: TOSCF2; ISSN: 1096-6080
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

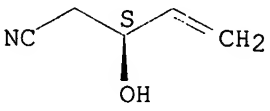
AB Indoles and isothiocyanates found in cruciferous vegetables have been implicated as chemopreventive agents against carcinogenesis. The bioactivities of chem. related cruciferous nitriles, including 1-cyano-2-hydroxy-3-butene (crambene), however, have not been thoroughly evaluated. Crambene causes a prolonged elevation of rat hepatic and **pancreatic** glutathione and induces the GSH S-transferases (GSTs). Because elevated GST activity against the model substrate chlorodinitrobenzene does not reflect individual isoenzyme induction, quant. HPLC evaluation of specific GST subunits is necessary to fully assess the range of GST isoenzymes induced by crambene. Accordingly, male Fischer 344 rats were given, via esophageal intubation, either 100 or 50 mg crambene/kg body wt once daily for 7 days. GSTs were extd. from hepatic cytosol by affinity chromatog., and the individual subunits that comprise the various isoenzymes were quantified by reverse-phase HPLC to gain an est. of induction. In addn., **pancreatic** GST subunits were assessed in the low-dose expt. In parallel with increased GST activity, crambene caused a generalized induction of GST subunits in both liver and **pancreas**, but the pattern of subunit induction was tissue dependent. In the liver, .alpha. subunits 1 and 2 and the .mu.

subunit 3 were induced approx. 2-fold, while the .mu. subunit 4 was induced only 1.5-fold. In the **pancreas**, the .alpha. subunit 2 was induced to a much larger extent (2.6-fold) than the other subunits (from no induction to 1.6 fold). These results suggests that crambene-mediated GST induction mechanisms vary from tissue to tissue. Potential chemoprevention provided by crambene against GST-metabolized carcinogens or toxins may differ between liver and **pancreas** because of differences in the degree and pattern of induction.

IT **6071-81-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(induction of hepatic and **pancreatic** glutathione S-transferases by crambene)

RN 6071-81-4 CAPLUS
CN 4-Pentenenitrile, 3-hydroxy-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

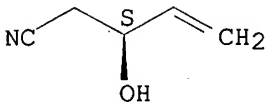
L57 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 6
ACCESSION NUMBER: 1998:800577 CAPLUS
DOCUMENT NUMBER: 130:48356
TITLE: Xenobiotic metabolism, oxidant stress, and chronic **pancreatitis**. Focus on glutathione
AUTHOR(S): Wallig, Matthew A.
CORPORATE SOURCE: Dep. Veterinary Pathobiology, College Veterinary Medicine, Univ. Illinois Urbana-Champaign, Urbana, IL, 61802, USA
SOURCE: Digestion (1998), 59(Suppl. 4), 13-24
CODEN: DIGEBW; ISSN: 0012-2823
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB Chronic **pancreatitis**, although relatively rare in the Western World, is common in certain tropical zones where staple crops such as cassava are rich in cyanogenic glycosides. The paper reviews 100 refs. the evidence for a cyanide connection, with ref. to exptl. studies using another plant nitrile, crambene; and then examines the hypothesis that chronic **pancreatitis** represents a manifestation of uncoordinated detoxification reactions between **pancreatic** cytochrome P 450 mono-oxygenases and phase II conjugating enzymes, resulting in the irreversible consumption of glutathione in the **acinar** cell. The conclusion is that the central role of disrupted **pancreatic** glutathione status, as a result of "xenobiotic stress", in the evolution of chronic **pancreatitis** cannot be overestimated. This position contrasts with that in acute **pancreatitis**, in which glutathione depletion has a pivotal role too, but occurs as a result of "stress" from reactive oxygen species.

IT **6071-81-4**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(role of glutathione in xenobiotic metab., oxidant stress, and chronic **pancreatitis**)

RN 6071-81-4 CAPLUS
CN 4-Pentenenitrile, 3-hydroxy-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



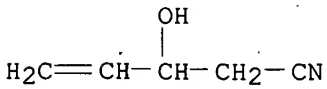
REFERENCE COUNT: 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L57 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 8
ACCESSION NUMBER: 1993:207183 CAPLUS
DOCUMENT NUMBER: 118:207183
TITLE: In vitro metabolism of cyanohydroxybutene: formation of a glutathione-S-transferase catalyzed product
AUTHOR(S): Davis, Myrtle A.; Wallig, Matthew A.; Jeffery, Elizabeth H.
CORPORATE SOURCE: Coll. Vet. Med., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Research Communications in Chemical Pathology and Pharmacology (1993), 79(3), 343-53
CODEN: RCOCB8; ISSN: 0034-5164
DOCUMENT TYPE: Journal
LANGUAGE: English

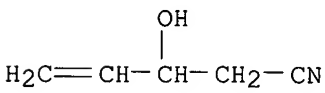
AB The **pancreatotoxin** cyanohydroxybutene (CHB) causes a significant and prolonged elevation in GSH in liver and **pancreas** (M. A. Wallig and E. H. Jeffery, 1990). Here the authors report that urinary thiols also increase. This suggests that CHB may react with GSH, either directly or following phase I oxidn., to form an adduct, which is further metabolized to the corresponding mercapturic acid for urinary excretion. Metab. of CHB by hepatic mixed-function oxidase and cytosolic alc. dehydrogenase enzymes was evaluated by monitoring microsomal NADPH consumption and alc. dehydrogenase-dependent NADH generation, resp. There was no apparent increase in the rate of microsomal NADPH consumption or alc. dehydrogenase-dependent NADH generation in the presence of CHB. To evaluate in vitro formation of a glutathione-S-transferase (GST)-catalyzed adduct, [3H-glycyl]GSH and [14C-cyano]CHB were incubated at 37.degree. for 1 h, with or without GST. Dinitrophenol derivatization and HPLC anal. (Farris, M.; Reed, D. J., 1987) revealed no double-labeled peaks, suggesting that no stable conjugate was formed. However a tritiated product, not present in control samples, and with an identical retention time to cysteinyl-glycine (cys-gly) was formed. In addn., the product has a fast atom bombardment mass-spectrum consistent with cys-gly. These results suggest that while CHB may not undergo phase I oxidn., in the presence of CHB, GSH may break down to form cys-gly. A mechanisms for CHB-dependent breakdown of GSH to cys-gly is proposed, and the pharmacol. implications of this finding are discussed.

IT **27451-36-1**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metab. of, glutathione and thiols in relation to)

RN 27451-36-1 CAPLUS
CN 4-Pentenenitrile, 3-hydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)



L57 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 9
ACCESSION NUMBER: 1994:25248 CAPLUS
DOCUMENT NUMBER: 120:25248
TITLE: Differential effect of cyanohydroxybutene on glutathione synthesis in liver and **pancreas** of male rats
AUTHOR(S): Dais, Myrtle A.; Wallig, Matthew A.; Eaton, David; Borroz, K. Ingrid; Jeffery, Elizabeth H.
CORPORATE SOURCE: Coll. Vet. Med., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Toxicology and Applied Pharmacology (1993), 123(2), 257-64
CODEN: TXAPA9; ISSN: 0041-008X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 1-Cyano-2-hydroxy-3-butene (CHB), an aliph. nitrile found in cruciferous vegetables, causes a two- and sevenfold elevation in reduced glutathione (GSH) in rat liver and **pancreas**, resp., after oral administration of 200 mg/kg. While this dose is also assocd. with **pancreatotoxicity**, a single 100 mg/kg dose or multiple lesser doses show the same effect, although somewhat reduced in magnitude, with no concomitant toxicity. In an attempt to identify the mechanism of this increase, the authors investigated the effect of CHB on GSH synthesis by examg. the effect of buthionine sulfoximine (BSO), an inhibitor of GSH synthesis, on CHB-induced GSH elevation. Male Fischer 344 rats received 3 mmol BSO/kg i.p. 24 and 334 h following CHB or corn oil. The CHB-mediated elevation in hepatic and **pancreatic** GSH was eradicated by BSO, suggesting that increased synthesis was responsible. The rate-limiting step in synthesis is .gamma.-glutamyl cysteine synthetase (GCS); the limiting substrate is cysteine. Therefore, CHB effects on GCS activity and hepatic and **pancreatic** cysteine equiv. were investigated. When rats were treated by gavage with CHB (100 mg/kg), hepatic GCS mRNA concns. were increased 24 h after treatment and hepatic cysteine equiv. were significantly elevated 4 h following CHB. No significant elevation in hepatic GCS activity was obsd., however, even 24 h following CHB. **Pancreatic** cysteine equiv. were elevated at both 4 and 8 h after CHB treatment. However, there was no detectable GCS mRNA or activity in **pancreas**, in either control or treated animals. Furthermore, CHB had no direct effect on the activity of GCS purified from kidney, regardless of whether GSH was present or absent. These results suggest that the mechanism of CHB-mediated induction of GSH may involve early increases in GSH precursors as well as a later increase in GCS mRNA. The mechanism of GSH elevation identified in these studies may hold therapeutic or prophylactic implications.
IT **27451-36-1**, 1-Cyano-2-hydroxy-3-butene
RL: BIOL (Biological study)
(glutathione of liver and **pancreas** response to)
RN 27451-36-1 CAPLUS
CN 4-Pentenenitrile, 3-hydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)



L57 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 10
ACCESSION NUMBER: 1993:53934 CAPLUS
DOCUMENT NUMBER: 118:53934
TITLE: Separation of the toxic and glutathione-enhancing effects of the naturally occurring nitrile, cyanohydroxybutene

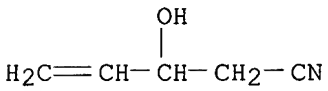
Searched by Barb O'Bryen, STIC 308-4291

AUTHOR(S): Wallig, Matthew A.; Kore, Anita M.; Crawshaw, Jacqueline; Jeffery, Elizabeth H.
CORPORATE SOURCE: Dep. Vet. Pathobiol., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Fundamental and Applied Toxicology (1992), 19(4), 598-606
CODEN: FAATDF; ISSN: 0272-0590
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cyanohydroxybutene (CHB) is hepatotoxic in male Fischer 344 rats at an oral dose of 300 mg/kg and, while no longer hepatotoxic, is **pancreatotoxic** at 200 mg/kg. In addn., the 200 mg/kg dose causes a persistent elevation in hepatic and **pancreatic** glutathione (GSH). This study was conducted to det. if smaller doses of CHB could cause GSH elevation in the absence of toxicity. A single oral dose of 100 mg/kg or multiple lower doses (50 mg/kg daily for 3 days or 30 mg/kg for 6 days) caused a significant and persistent increase in **pancreatic** GSH, although hepatic levels were unchanged. Ten milligrams per kg, even daily for 24 days, was without effect on hepatic or **pancreatic** GSH. Neither a single oral dose of 100 mg/kg nor multiple lower doses were assocd. with toxicity. However, when either 100 or 50 mg/kg were administered i.v., **pancreatic** apoptosis was obsd. In animals dosed with 100 mg/kg i.v., mixed histiocytic and suppurative inflammation and frank **pancreatic** necrosis also developed and were assocd. with elevated plasma lipase and amylase. The animals receiving CHB i.v. also exhibited elevated GSH levels in both **pancreas** and liver. This study shows that oral doses between 30 and 100 mg CHB/kg can be used to elevate GSH levels without any **pancreatotoxicity**. However, a single 50 mg CHB/kg dose given i.v. causes apoptosis, while 100 mg/kg causes sèvere **pancreatotoxicity** with necrosis.

IT **27451-36-1**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(toxicity of, to **pancreas**)

RN 27451-36-1 CAPLUS
CN 4-Pentenenitrile, 3-hydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)



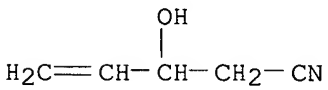
L57 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 15
ACCESSION NUMBER: 1990:156886 CAPLUS
DOCUMENT NUMBER: 112:156886
TITLE: Enhancement of **pancreatic** and hepatic glutathione levels in rats during cyanohydroxybutene intoxication
AUTHOR(S): Wallig, Matthew A.; Jeffery, Elizabeth H.
CORPORATE SOURCE: Coll. Vet. Med., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: Fundamental and Applied Toxicology (1990), 14(1), 144-59
CODEN: FAATDF; ISSN: 0272-0590
DOCUMENT TYPE: Journal
LANGUAGE: English

105

AB 1-Cyano-2-hydroxy-3-butene (CHB), a product of glucosinolates in crucier autolysis, is hepatotoxic, **pancreatotoxic**, and elevates glutathione (GSH) in liver and **pancreas**. Whether GSH elevation is preceded by a depletion related to toxicity, or whether toxicity and GSH elevation are unrelated, is not known. To evaluate the temporal relationship between toxicity and GSH levels, male Fisher 344 rats

(6/group) were given CHB (200 mg/kg orally) and killed up to 96 h after dosing. Histol. and ultrastructural evaluations and GSH/GSSG detns. were performed on liver and **pancreas**. In **pancreas**, dilation of the cisternae of the rough endoplasmic reticulum was evident from 2 h, becoming progressively more severe 4 and 6 h after CHB. Frank apoptosis and loss of zymogen granules was evident by 6 h, becoming widespread by 12 h. Recovery had commenced by 72 h, and 50% of treated rats had normal **pancreases** by 96 h. No hepatic lesions were obsd. at this dose. **Pancreatic** GSH was depressed to <20% at 2 and 4 h, rose to a max. of 540% by 12 h, and remained elevated in treated rats throughout the study (275% at 96 h). Hepatic GSH fell to 50%, rose to 150-180%, and returned to normal by 96 h. Althouth this pattern of depletion and rebound following exposure to hepatotoxins is common, the exaggerated and persistent elevation of **pancreatic** GSH is unprecedented.

IT **27451-36-1**
RL: BIOL (Biological study)
(glutathione and morphol. of liver and **pancreas** response to dietary)
RN 27451-36-1 CAPLUS
CN 4-Pentenenitrile, 3-hydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

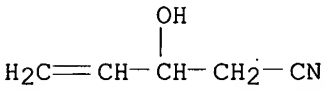


L57 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 16
ACCESSION NUMBER: 1989:211172 CAPLUS
DOCUMENT NUMBER: 110:211172
TITLE: The relationship of vehicle to target organ toxicology induced by the naturally occurring nitrile 1-cyano-2-hydroxy-3-butene
AUTHOR(S): Wallig, Matthew A.; Gould, Daniel H.; Van Steenhouse, Jan; Fettman, Martin J.; Willhite, Calvin C.
CORPORATE SOURCE: Dep. Pathol., Colorado State Univ., Fort Collins, CO, 80523, USA
SOURCE: Fundamental and Applied Toxicology (1989), 12(3), 377-85
CODEN: FAATDF; ISSN: 0272-0590
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of gavage vehicle on the acute toxicity of the naturally occurring nitrile 1-cyano-2-hydroxy-3-butene (CHB) were investigated by oral administration of 200 mg/kg body wt./day CHB to male CDF (F-344/Crl BR) rats for 2 days. The vehicles studied were distd. water, 5% aq. Tween 20, and corn oil. Liver, kidney, and **pancreas** were examd. histol. and the differences in lesion incidence and severity were assessed. The effects of gavage vehicle on nitrile-induced elevations of daily urinary thiocyanate excretion and tissue glutathione concns. were also assessed. The **pancreatotoxicity** of CHB was present regardless of vehicle and consisted of apoptosis of **pancreatic acinar** cells, infiltration of **pancreatic** lobules by macrophages, and **acinar** atrophy and disorganization. CHB in water alone was assocd. with the least **pancreatotoxic** effect, whereas the aq. Tween vehicle was assocd. with more severe CHB-induced **pancreatic** lesions. CHB-induced elevations of tissue nonprotein thiol and glutathione concns. occurred in all treatment groups, but the values were elevated less in the **pancreata** of CHB-Tween-treated rats than in those of rats given CHB in water or corn oil. By contrast, the greatest elevation in daily urinary thiocyanate excretion occurred in

rats given CHB in aq. Tween, indicating increased biotransformation of CHB to cyanide when Tween 20 was used as a vehicle. These results illustrate the difficulty of identifying suitable vehicles for administration of lipophilic compds. in toxicol. studies.

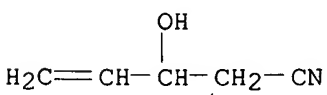
IT **27451-36-1**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(toxicol. testing of, vehicle-target organ relations in)
RN 27451-36-1 CAPLUS
CN 4-Pentenenitrile, 3-hydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)



L57 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 17
ACCESSION NUMBER: 1988:418345 CAPLUS
DOCUMENT NUMBER: 109:18345
TITLE: Selective **pancreatotoxicity** in the rat induced by the naturally occurring plant nitrile 1-cyano-2-hydroxy-3-butene
AUTHOR(S): Wallig, M. A.; Gould, D. H.; Fettman, M. J.
CORPORATE SOURCE: Coll. Vet. Med. Biomed. Sci., Colorado State Univ., Fort Collins, CO, 80523, USA
SOURCE: Food and Chemical Toxicology (1988), 26(2), 137-47
CODEN: FCTOD7; ISSN: 0278-6915
DOCUMENT TYPE: Journal
LANGUAGE: English

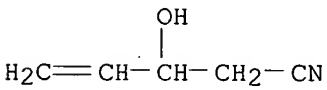
AB The acute toxicity of 1-cyano-2-hydroxy-3-butene (CHB), a nitrile derived from many cruciferous plants, was investigated. Young male rats were treated by gavage once daily with 200 mg (2.1 mmol) CHB/kg for 0.4 days and killed 24 h after the final dose. Lesions were confined to the exocrine **pancreas** and characterized by individual **acinar** cell death, inflammation and **acinar** atrophy and disorganization. Ultrastructural alterations included dilation of cisternae of the **acinar** cell endoplasmic reticulum, **acinar** cell death resembling apoptosis, macrophage phagocytosis of **acinar** cell debris and regenerative changes in remaining **acinar** cells. **Pancreatic**, hepatic and renal nonprotein thiol concns. were elevated, suggesting an enhancement of tissue glutathione concns. and an alteration in glutathione metab. Urinary thiocyanate excretion was modestly elevated, indicating some in vivo cyanide release from this nitrile. The results of this study indicate that CHB is a selective **pancreatotoxin**, inducing changes consistent with apoptosis. CHB is also a possible inducer of tissue glutathione in the liver and kidneys as well as in the **pancreas**, even at toxic doses.

IT **27451-36-1**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(toxicity of, to **pancreas**)
RN 27451-36-1 CAPLUS
CN 4-Pentenenitrile, 3-hydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)



L57 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:312924 CAPLUS

DOCUMENT NUMBER: 127:379
TITLE: Evaluation of the induction of rat hepatic and **pancreatic** glutathione S-transferases by treatment with the cruciferous nitrile, cyanohydroxybutene
AUTHOR(S): March, Thomas Hugh
CORPORATE SOURCE: Univ. of Illinois, Urbana, IL, USA
SOURCE: (1996) 240 pp. Avail.: Univ. Microfilms Int., Order No. DA9712368
From: Diss. Abstr. Int., B 1997, 57(11), 6863
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT **27451-36-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cyanohydroxybutene induction of hepatic and **pancreatic** glutathione S-transferases)
RN 27451-36-1 CAPLUS
CN 4-Pentenenitrile, 3-hydroxy- (7CI, 8CI, 9CI) (CA INDEX NAME)



L57 ANSWER 13 OF 23 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000050292 MEDLINE
DOCUMENT NUMBER: 20050292 PubMed ID: 10583631
TITLE: Massive acinar cell apoptosis with secondary necrosis, origin of ducts in atrophic lobules and failure to regenerate in **cyanohydroxybutene** pancreatopathy in rats.
AUTHOR: Kelly L; Reid L; Walker N I
CORPORATE SOURCE: Department of Pathology, University of Queensland, Herston, Australia.
SOURCE: INTERNATIONAL JOURNAL OF EXPERIMENTAL PATHOLOGY, (1999 Aug) 80 (4) 217-26.
Journal code: 9014042. ISSN: 0959-9673.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991223

ABSTRACT:
Cyanohydroxybutene (CHB), a glycosinolate breakdown product, causes pancreatic injury when given to animals in large amounts. To determine the course of CHB-induced pancreatopathy, rats were given a single subcutaneous dose of CHB and the pancreas weighed and examined by light and electron microscopy and immunohistochemistry at intervals from 2 h to 28 days. The pancreatic lesion was unusual in that there was marked early oedema with limited inflammatory cell infiltration, rapid synchronous onset of acinar cell apoptosis and early advanced atrophy engendering only a limited regenerative response. Acinar cell apoptosis was atypical in that cell fragmentation was limited and phagocytosis delayed, resulting in extensive secondary necrosis.

As ducts were unaffected by CHB, the crowded ducts making up the epithelial component of atrophic lobules could be clearly shown to derive from their condensation and proliferation, not the redifferentiation of pre-existing acinar cells, widely held to produce this lesion. Although the basis of CHB selectivity and toxicity for pancreatic acinar cells remains unknown, the potential therapeutic benefit of such an agent in patients with pancreatitis or pancreatic tumours warrants further investigation.

CONTROLLED TERM: Check Tags: Animal; Male
*Apoptosis: DE, drug effects
*Butanols: TO, toxicity
Disease Progression
Microscopy, Electron
Necrosis
***Pancreas: PA, pathology**
Pancreas: PH, physiology
Pancreas: UL, ultrastructure
***Pancreatic Diseases: CI, chemically induced**
Pancreatic Diseases: PA, pathology
Rats
Rats, Wistar
Regeneration

CAS REGISTRY NO.: 671-56-7 (1-chloro-2-hydroxy-3-butene)
CHEMICAL NAME: 0 (Butanols)

L57 ANSWER 14 OF 23 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 97187134 MEDLINE
DOCUMENT NUMBER: 97187134 PubMed ID: 9034587
TITLE: Studies on the toxic effects of crambe meal and two of its constituents, 1-cyano-2-hydroxy-3-butene (CHB) and epi-progoitrin, in broiler chick diets.
AUTHOR: Kloss P; Jeffery E; Tumbleson M; Zhang Y; Parsons C; Wallig M
CORPORATE SOURCE: Division of Nutritional Sciences, University of Illinois, Urbana 61801, USA.
SOURCE: BRITISH POULTRY SCIENCE, (1996 Dec) 37 (5) 971-86.
Journal code: 15740290R. ISSN: 0007-1668.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970514
Last Updated on STN: 19980206
Entered Medline: 19970508

ABSTRACT:
1. Studies were undertaken to determine a safe inclusion rate for crambe (Crambe abyssinica) meal in broiler chick diets, and to determine the mechanism for adverse effects by investigating its constituents; 1-cyano-2-hydroxy-3-butene (CHB) and 3-butenyl glucosinolate (epi-progoitrin, E-PG). 2. Crambe meals were prepared to differ in E-PG (19, 36 and 40 g/kg) and CHB contents (0.1, 0.7 and 1.9 g/kg), and with either active or inactive thioglucosidase. 3. Meals were fed to 7-d-old broiler chicks at 50 or 100 g/kg of the diet for 12 or 13 d. In separate studies, isolated E-PG or CHB were mixed into the diet or administered by gavage to 7-d-old broiler chicks in amounts equivalent to 50 or 100 g/kg crambe meal diets for 10 and 12 d, respectively. 4. Weight gain decreased ($P < 0.05$) in chicks fed on the high glucosinolate crambe diets or isolated E-PG. Food consumption decreased ($P < 0.05$) in chicks fed on the diet containing the high E-PG meal with active enzyme. 5. Mild liver lesions and increased serum aspartate aminotransferase were found in chicks fed on the diet containing the high glucosinolate meal with active enzyme. Other organs, including thyroids, were normal. 6. Commercially-processed crambe meal appeared safe at an inclusion rate of 50 or 100 g/kg diet, but could not be recommended at this point for long term feeding.

CONTROLLED TERM: Check Tags: Animal; Female; Male; Support, U.S. Gov't, Non-P.H.S.
*Alkenes: AE, adverse effects
Aspartate Aminotransferases: BL, blood
Chickens: BL, blood
*Chickens: PH, physiology
Diet: ST, standards
*Diet: VE, veterinary
*Dietary Proteins: AE, adverse effects
Eating: PH, physiology
*Glucosinolates: AE, adverse effects
Kidney: DE, drug effects
Kidney: PA, pathology
Liver: DE, drug effects
Liver: PA, pathology
*Nitriles: AE, adverse effects
Pancreas: DE, drug effects
Pancreas: PA, pathology
*Plant Proteins: AE, adverse effects
Soybeans: ST, standards
Weight Gain: PH, physiology
Zea mays: ST, standards

structure printed at beginning of search

CAS REGISTRY NO.: **27451-36-1 (1-cyano-2-hydroxy-3-butene)**; 585-95-5 (progoitrin); 78783-34-3 (crambin protein, Crambe abyssinica)
CHEMICAL NAME: 0 (Alkenes); 0 (Dietary Proteins); 0 (Glucosinolates); 0 (Nitriles); 0 (Plant Proteins); EC 2.6.1.1 (Aspartate Aminotransferases)

L57 ANSWER 15 OF 23 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 91360572 MEDLINE
DOCUMENT NUMBER: 91360572 PubMed ID: 1886886
TITLE: The acute pancreatotoxic effects of the plant nitrile 1-cyano-2-hydroxy-3-butene.
AUTHOR: Maher M; Chernenko G; Barrowman J A
CORPORATE SOURCE: Faculty of Medicine, Memorial University of Newfoundland, St. John's, Canada.
SOURCE: PANCREAS, (1991 Mar) 6 (2) 168-74.
Journal code: 8608542. ISSN: 0885-3177.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199110
ENTRY DATE: Entered STN: 19911027
Last Updated on STN: 19980206
Entered Medline: 19911004

ABSTRACT:
The effects of synthetic 1-cyano-2-hydroxy-3-butene (CHB), a racemic mixture of the (R)- and (S)-enantiomers, were studied in adult male rats. The compound given by gavage in olive oil at doses of 25-200 mg/kg causes toxic effects on the pancreas that resemble those seen when naturally occurring CHB is given to rats. At 6 h after dosing, pancreatic edema is seen with doses of 100 mg/kg and greater. The edema fluid had a high protein content, indicating a marked increase in macromolecular permeability of the pancreatic microcirculation. A loss of zymogen granules from the acinar cells and a lacy supranuclear vacuolation of the acinar cell cytoplasm was observed. At 4 h after dosing, pancreatic nonprotein thiols were depleted and rebounded at 24 h to three times control values. At 120 h nonprotein thiol levels decreased but were still elevated compared with control values. Glutathione-S-transferase activity in the pancreas had a similar pattern of change with initial reduction, followed by elevation at 24 h. In rats with pancreatic and biliary fistulas, intraduodenal CHB caused a transient early stimulation of pancreatic juice

secretion followed by a return to control values in the case of the lower doses of CHB and depression of flows at larger doses. All doses of CHB caused a dose-related depression of protein concentration in pancreatic juice. Pancreatic juice flow was almost abolished at doses of 200 mg/kg. CHB caused a dose-dependent choleresis accompanied by a marked reduction in bile acid concentrations in bile.(ABSTRACT TRUNCATED AT 250 WORDS)

CONTROLLED TERM: Check Tags: Animal; Comparative Study; Male; Support, Non-U.S. Gov't
Acute Disease
*Alkenes: TO, toxicity
Glutathione: ME, metabolism
Glutathione Transferase: ME, metabolism
*Nitriles: TO, toxicity
***Pancreatic Diseases: CI, chemically induced**
*Plant Extracts: TO, toxicity
Rats
Rats, Inbred Strains
Stereoisomerism

CAS REGISTRY NO.: 27451-36-1 **(1-cyano-2-hydroxy-3-butene)**; 70-18-8 (Glutathione)

CHEMICAL NAME: 0 (Alkenes); 0 (Nitriles); 0 (Plant Extracts); EC 2.5.1.18 (Glutathione Transferase)

L57 ANSWER 16 OF 23 DRUGU COPYRIGHT 2003 THOMSON DERWENT

ACCESSION NUMBER: 1997-25767 DRUGU P

TITLE: Induction of apoptosis in mouse **pancreatic acinar** cells with 1-**cyano**-2-**hydroxy**-3-**butene** (CHB) reduces the severity of caerulein-induced **pancreatitis**.

AUTHOR: Bhatia M; Saluja A; Wallig M; Hofbauer B; Lee H S; Frossard J L; Wattanga H; Steer M

CORPORATE SOURCE: Univ.Harvard; Univ.Illinois

LOCATION: Boston; Beth Israel, Mass.; Urbana, Ill., USA

SOURCE: Gastroenterology (112, No. 4, Suppl., A428, 1997)
CODEN: GASTAB ISSN: 0016-5085

AVAIL. OF DOC.: Beth Israel Deaconess Medical Center, Beth Israel, U.S.A.

LANGUAGE: English

DOCUMENT TYPE: Journal

ABSTRACT:

The effects of i.v. 1-**cyano**-2-**hydroxy**-3-**butene** (CHB) on development of i.p. caerulein-induced acute **pancreatitis** were evaluated in mice.In mice administered CHB, the severity of ***pancreatitis*** was significantly reduced. Maximal protection was observed in mice in which caerulein treatment was started 12 hours after CHB administration. These observations indicate that apoptosis of **acinar** cells induced by CHB results in reduced severity of acute **pancreatitis** induced by caerulein in mice. These results support the hypothesis that apoptosis acts as a protective mechanism against **pancreatitis** and suggest the potential benefits of the induction of apoptosis as a prophylactic/therapeutic strategy for acute **pancreatitis**. (conference abstract).

SECTION HEADING: P Pharmacology

CLASSIF. CODE: 16 Gastrointestinal

CONTROLLED TERM:

[01] DR9704797 *RN; ACUTE *OC; **PANCREATITIS** *OC; **PANCREOPATHY** *OC; CERULETIDE *RC; I.V. *FT; IN-VIVO *FT; MOUSE *FT; APOPTOSIS *FT; **ACINAR**-CELL *FT; MODE-OF-ACT. *FT; NEW *FT; INJECTION *FT; LAB.ANIMAL *FT; PH

*FT
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L57 ANSWER 17 OF 23 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 11
ACCESSION NUMBER: 1991:330928 BIOSIS
DOCUMENT NUMBER: BR41:27478
TITLE: TOXICITY DISTRIBUTION AND ELIMINATION OF INTRAVENOUS **CYANOHYDROXYBUTENE** CHB.
AUTHOR(S): KORE A M; MARCH T H; DAVIS M A; JEFFERY E H; WALLIG M A
CORPORATE SOURCE: UNIV. ILL., URBANA, ILL. 61801.
SOURCE: 75TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ATLANTA, GEORGIA, USA, APRIL 21-25, 1991. FASEB (FED AM SOC EXP BIOL) J, (1991) 5 (6), A1571.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English
CONCEPT CODE: General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Biochemical Studies - General 10060
Metabolism - General Metabolism; Metabolic Pathways *13002
Endocrine System - Pancreas *17008
Toxicology - General; Methods and Experimental *22501
BIOSYSTEMATIC CODE: Muridae 86375
INDEX TERMS: Miscellaneous Descriptors
ABSTRACT RAT **PANCREATOTOXIN** TOXICOKINETICS

L57 ANSWER 18 OF 23 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 13
ACCESSION NUMBER: 1990:345201 BIOSIS
DOCUMENT NUMBER: BR39:40462
TITLE: 1 **CYANO**-2-**HYDROXY**-3-**BUTENE**
CHB A POTENT **PANCREATOTOXIC** PLANT-DERIVED NITRILE.
AUTHOR(S): MAHER M; CHERNENKO G; BARROWMAN J A
CORPORATE SOURCE: FAC. MED., MEML. UNIV. NEWFOUNDLAND, ST. JOHN'S, NEWFOUNDLAND, CAN.
SOURCE: ABSTRACTS OF PAPERS SUBMITTED TO THE AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES FOR THE 91ST ANNUAL MEETING OF THE AMERICAN GASTROENTEROLOGICAL ASSOCIATION, SAN ANTONIO, TEXAS, USA, MAY 12-18, 1990. GASTROENTEROLOGY, (1990) 98 (5 PART 2), A662.
CODEN: GASTAB. ISSN: 0016-5085.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English
CONCEPT CODE: General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Necrosis *12510
Metabolism - General Metabolism; Metabolic Pathways 13002
Metabolism - Proteins, Peptides and Amino Acids *13012
Digestive System - Pathology *14006
Toxicology - General; Methods and Experimental *22501
Laboratory Animals - General 28002
Plant Physiology, Biochemistry and Biophysics - Chemical

Constituents *51522
Pharmacognosy and Pharmaceutical Botany *54000
BIOSYSTEMATIC CODE: Cruciferae 25880
Muridae 86375
INDEX TERMS: Miscellaneous Descriptors
ABSTRACT RAT CRUCIFEROUS PLANTS NON-PROTEIN THIOLS GLUTATHIONE GLUTATHIONE-S-TRANSFERASE **ACINAR** CELL DEATH HYPERSECRETION TOXIC **PANCREATIC** INJURY MODEL
REGISTRY NUMBER: 70-18-8 (GLUTATHIONE)
50812-37-8 (GLUTATHIONE-S-TRANSFERASE)

L57 ANSWER 19 OF 23 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 14
ACCESSION NUMBER: 1991:83072 BIOSIS
DOCUMENT NUMBER: BR40:37057
TITLE: **PANCREATIC** TOXICITY OF THE PLANT NITRILE 1 **CYANO**-2-**HYDROXY**-3-**BUTENE**.
AUTHOR(S): MAHER M; CHERNENKO G; BARROWMAN J A
CORPORATE SOURCE: FAC. MED., MEML. UNIV. NEWFOUNDLAND, ST. JOHN'S NEWFOUNDLAND, CANADA.
SOURCE: XXIIND MEETING OF THE EPC (EUROPEAN PANCREATIC CLUB), BASEL, SWITZERLAND, OCTOBER 15-17, 1990. DIGESTION, (1990) 46 (3), 156-157.
CODEN: DIGEBW. ISSN: 0012-2823.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English
CONCEPT CODE: General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses; Review Annuals 00520
Biochemical Studies - General 10060
Digestive System - Pathology *14006
Endocrine System - Pancreas *17008
Toxicology - General; Methods and Experimental *22501
Plant Physiology, Biochemistry and Biophysics - Chemical Constituents *51522
BIOSYSTEMATIC CODE: Muridae 86375
INDEX TERMS: Miscellaneous Descriptors
ABSTRACT RAT

L57 ANSWER 20 OF 23 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:318117 BIOSIS
DOCUMENT NUMBER: PREV199800318117
TITLE: Induction of rat **pancreatic** glutathione S-transferase and quinone reductase activities by a mixture of glucosinolate breakdown derivatives found in brussels sprouts.
AUTHOR(S): Wallig, M. A. (1); Kingston, S.; Staack, R.; Jeffery, E. H.
CORPORATE SOURCE: (1) Dep. Vet. Pathobiol., 2001 S. Lincoln Ave., Urbana, IL 61802 USA
SOURCE: Food and Chemical Toxicology, (May, 1998) Vol. 36, No. 5, pp. 265-373.
ISSN: 0278-6915.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:
The chemoprotective effects of cruciferous vegetables against cancer has been linked to the induction of detoxification enzymes, including the phase II enzymes, glutathione S-transferases (GST) and quinone reductase (QR). Four glucosinolate breakdown products found in Brussels sprouts and previously shown individually to affect detoxification enzymes-(1-**cyano**-2-***hydroxy*** -3-**butene** (Crambene), indole-3-carbinol (I3C), phenylethyl isothiocyanate (PEITC) and 1-isothiocyanato-3-(methylsulfinyl)-

propane (IBN)-were administered to male F344 rats by oesophageal intubation for 7 days both as a mixture and individually to assess the effect of these compounds on GST and QR activity in the **pancreas**, an organ previously shown to be affected by cruciferous diets. The doses of each compound in the mixture (50 mg Crambene/kg, 56 mg I3C/kg, 0.1 mg PEITC/kg and 38 mg IBN/kg) were chosen to represent the relative proportions of the parent glucosinolate for each compound in Brussels sprouts and shown to be below the toxic threshold for all the compounds. In rats receiving the mixture, ***pancreatic*** QR and GST activities were elevated 31- and 1.7-fold, respectively, while glutathione (GSH) was elevated threefold. On an individual basis, Crambene alone caused a 21-fold elevation of QR and 1.5-fold elevation of GST activities, while **pancreatic** GSH was elevated by both Crambene and PEITC 2.6- and twofold, respectively. No other significant effects of individual components were found. When the mixture was administered at 60% of the original dose, **pancreatic** QR and GST activities were elevated 12- and 1.4-fold, respectively, and **pancreatic** GSH was elevated 1.5-fold. At 20% of the original dose, **pancreatic** GSH was unaffected and QR and GST activities were elevated 2.7- and 1.3-fold, respectively. The results of these studies suggest that a diet rich in cruciferous vegetables may produce phase II enzyme induction in the **pancreas**, and that Crambene may be the most active component.

CONCEPT CODE: Food Technology - General; Methods *13502
Biochemical Studies - General *10060
Enzymes - General and Comparative Studies; Coenzymes *10802
Digestive System - General; Methods *14001
Endocrine System - General *17002
Neoplasms and Neoplastic Agents - General *24002

BIOSYSTEMATIC CODE: Muridae 86375

INDEX TERMS: Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Foods

INDEX TERMS: Parts, Structures, & Systems of Organisms
pancreas: digestive system, endocrine system

INDEX TERMS: Diseases
cancer: neoplastic disease

INDEX TERMS: Chemicals & Biochemicals
glutathione; glutathione-S-transferase: detoxification enzyme, induction; indole-3-carbinol: brussels sprouts constituent; phenylethyl isothiocyanate: brussels sprouts constituent; quinone reductase: detoxification enzyme, induction; 1-**cyano**-2-**hydroxy**-3-**butene** [Crambene]: brussels sprouts constituent; 1-isothiocyanato-3-(methylsulfinyl)-propane: brussels sprouts constituent

INDEX TERMS: Miscellaneous Descriptors
brussels sprouts: chemopreventive effect, vegetable

ORGANISM: Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGANISM: Organism Name
F344 rat (Muridae): male

ORGANISM: Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

REGISTRY NUMBER: 50812-37-8 (GLUTATHIONE S-TRANSFERASE)
9032-20-6 (QUINONE REDUCTASE)
70-18-8 (GLUTATHIONE)
700-06-1 (INDOLE-3-CARBINOL)

L57 ANSWER 21 OF 23 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:421498 BIOSIS
DOCUMENT NUMBER: PREV199799720701
TITLE: 1-**Cyano**-2-**hydroxy**-3-**butene** (CHB) induces apoptosis in mouse **pancreatic**

acinar cells and reduces the severity of **pancreatitis**.
AUTHOR(S): Bhatia, M.; Saluja, A. K.; Wallig, M.; Hofbauer, B.; Lee, H. S.; Frossard, J. L.; Steer, M. L.
CORPORATE SOURCE: Harvard Med. Sch., Beth Israel Deaconess Med. Cent., Boston, MA USA
SOURCE: FASEB Journal, (1997) Vol. 11, No. 9, pp. A1239.
Meeting Info.: 17th International Congress of Biochemistry and Molecular Biology in conjunction with the Annual Meeting of the American Society for Biochemistry and Molecular Biology San Francisco, California, USA August 24-29, 1997
ISSN: 0892-6638.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English
CONCEPT CODE: General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Cytology and Cytochemistry - Animal *02506
Genetics and Cytogenetics - Animal *03506
Replication, Transcription, Translation *10300
Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease *12508
Pathology, General and Miscellaneous - Necrosis *12510
Pathology, General and Miscellaneous - Therapy *12512
Digestive System - Pathology *14006
Endocrine System - Pancreas *17008
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Pharmacology - Digestive System *22014
Developmental Biology - Embryology - Morphogenesis, General *25508
In Vitro Studies, Cellular and Subcellular *32600
BIOSYSTEMATIC CODE: Muridae *86375
INDEX TERMS: Major Concepts
Cell Biology; Development; Digestive System (Ingestion and Assimilation); Endocrine System (Chemical Coordination and Homeostasis); Genetics; Molecular Genetics (Biochemistry and Molecular Biophysics); Pathology; Pharmacology
INDEX TERMS: Miscellaneous Descriptors
APOPTOSIS; APOPTOSIS INDUCER; CELL BIOLOGY; CHB; DIGESTIVE SYSTEM; DIGESTIVE SYSTEM DISEASE; ENDOCRINE SYSTEM; METABOLIC-DRUG; **PANCREATIC ACINAR** CELLS; **PANCREATITIS**; PHARMACODYNAMICS; PHARMACOLOGY; PROGRAMMED CELL DEATH; 1-**CYANO**-2-**HYDROXY**-3-**BUTENE**
ORGANISM: Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISM: Organism Name
mouse (Muridae)
ORGANISM: Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates

L57 ANSWER 22 OF 23 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:278631 BIOSIS
DOCUMENT NUMBER: PREV199799577834
TITLE: Induction of apoptosis in mouse **pancreatic acinar** cells with 1-**cyano**-2-**hydroxy**-3-**butene** (CHB) reduces the severity of caerulein-induced **pancreatitis**.
AUTHOR(S): Bhatia, M.; Saluja, A.; Wallig, M.; Hofbauer, B.; Lee, H.-S.; Frossard, J.-L.; Wattanga, H.; Steer, M.
CORPORATE SOURCE: Beth Israel Deaconess Med. Cent., Harvard Med. Sch.,

Boston, MA USA
SOURCE: Gastroenterology, (1997) Vol. 112, No. 4 SUPPL., pp. A428.
Meeting Info.: Digestive Disease Week and the 97th Annual Meeting of the American Gastroenterological Association Washington, D.C., USA May 11-14, 1997
ISSN: 0016-5085.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English
CONCEPT CODE: Pathology, General and Miscellaneous - Therapy *12512
Digestive System - General; Methods *14001
Pharmacognosy and Pharmaceutical Botany *54000
BIOSYSTEMATIC CODE: Muridae *86375
INDEX TERMS: Major Concepts
Digestive System (Ingestion and Assimilation); Pathology; Pharmacognosy (Pharmacology)
INDEX TERMS: Chemicals & Biochemicals
CAERULEIN; CERULEIN
INDEX TERMS: Miscellaneous Descriptors
ANIMAL MODEL; APOPTOSIS; CERULEIN; CRUCIFEROUS PLANT NITRILE; DIGESTIVE SYSTEM; DIGESTIVE SYSTEM DISEASE; DRUG-INDUCED; **PANCREATIC ACINAR** CELL; **PANCREATITIS**; PHARMACOGNOSY; SEVERITY; 1-**CYANO**-2-**HYDROXY**-3-**BUTENE**
ORGANISM: Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISM: Organism Name
mouse (Muridae)
ORGANISM: Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
REGISTRY NUMBER: 17650-98-5 (CAERULEIN)
17650-98-5 (CERULEIN)

L57 ANSWER 23 OF 23 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1991:287141 BIOSIS
DOCUMENT NUMBER: BR41:7561
TITLE: DAILY ADMINISTRATION OF LOW DOSES OF THE CRUCIFEROUS NITRILE **CYANOHYDROXYBUTENE** CHB CAUSES **PANCREATIC** GLUTATHIONE GSH ELEVATION.
AUTHOR(S): WALLIG M A; MARCH T H; KORE A M; JEFFERY E H
CORPORATE SOURCE: UNIV. ILL., URBANA, ILL. 61801.
SOURCE: 75TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ATLANTA, GEORGIA, USA, APRIL 21-25, 1991. FASEB (FED AM SOC EXP BIOL) J, (1991) 5 (5), A932.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English
CONCEPT CODE: General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Carbohydrates 10068
Metabolism - Proteins, Peptides and Amino Acids *13012
Digestive System - Physiology and Biochemistry *14004
Endocrine System - Pancreas 17008
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Routes of Immunization, Infection and Therapy 22100
Plant Physiology, Biochemistry and Biophysics - Chemical Constituents 51522
Pharmacognosy and Pharmaceutical Botany 54000

BIOSYSTEMATIC CODE: Muridae 86375
INDEX TERMS: Miscellaneous Descriptors
ABSTRACT RAT METABOLIC-DRUG
REGISTRY NUMBER: 70-18-8 (GLUTATHIONE)
70-18-8 (GSH)

=> fil hom
FILE 'HOME' ENTERED AT 15:09:06 ON 28 APR 2003